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1995 ASHG PRESIDENTIAL ADDRESS
The Challenges and Opportunities of Times of Change

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I have been deeply honored to have been your president for the year of 1995. It is the midyear of the last decade of the 20th century. It is a time in North America when we are seeing change at an ever-increasing pace. In every period of history, people have thought their time to be the most complex. "It was the best of times, it was the worst of times." In this "our" time, we also have enormous challenges and amazing opportunities.

There is a Chinese curse that is variably translated as "may you live in times of change" or "may you live in interesting times." Both are clearly true of our time. Perhaps change is not really a curse, but is rather a time for prioritization and innovation. With change comes the opportunity to develop different patterns of activities, new insights, and broader understanding and to undertake new responsibilities.

Giving a presidential address is a nerve-wracking responsibility. In reviewing what other presidents have said, I found that some had reflected on who they were personally, revealing their philosophies; some had reviewed their research; and some had reported on the state and direction of our society, while still others reflected on the fundamental nature of the broader social fabric (Muller 1950; Dunn 1962; McKusick 1975, 1992; Hamerton 1976; Childs 1977; Motulsky 1978; Knudson 1979; Rosenberg 1981; Shaw 1984; Littlefield 1984; Scriver 1987; Comings 1989; Caskey 1991; Nance 1993; Rowley 1994; Cohen 1995). I plan to focus on the opportunities within this time of change. Undoubtedly my own philosophy will be revealed as I describe major change for clinical genetics and for the type of research conducted in clinical genetics. I will also discuss my interest and work on the nontraditional mechanisms of genetic disorders and natural history of genetic diseases as they reflect a changing perspective in human genetic research. Last, but not least, I will outline how The American Society of Human Genetics is responding to the changes around us.

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I should explain at the very beginning that I am a clinician researcher, a Canadian immigrant, and a woman who has lived through the last half century in North America. Since each member of The American Society of Human Genetics represents several areas of interest, I think it is appropriate to acknowledge the different groups that I represent. The strength of our Society comes from the existence of many different types of geneticists within it, the many different perspectives they bring, the marvelous interactions that occur, and the conscious decision that we have made to group ourselves together as human geneticists and to support and collaborate with each other.

A discussion of the theme of change and diversity would be incomplete without stressing the value of nontraditional and innovative ways of thinking and acting. Evolutionary geneticists point out that the success of human beings in the course of evolution has been due to their flexibility and adaptability. It seems fitting to emphasize that the vitality of The American Society of Human Genetics also comes from hybrid vigor and diversity.

Clinical Genetics

I want to address being a clinical geneticist, first, and to emphasize how much there is yet to be learned in this field. Clinical genetics is the application of the principles of human genetics and basic genetics to human variation and disease processes. Thus, the clinical geneticist is meant to take the new knowledge that have been developed in various areas of genetics and translate it into useful, practical, and meaningful information for patients and families. Families often feel completely bewildered when a congenital anomaly or genetic disorder is recognized in their family. The diagnosis usually has a disorienting impact on the whole family, leaving them without their usual support systems or sense of security. Not only is the health care system intimidating, but the public's concept of genetics is somewhere between *Brave New World* and *Star Trek*. New information pouring out of laboratories is leading to new classifications, innovative therapies, and high expectations by families. It is a real challenge to provide information in an understandable way that helps the family deal with their questions and issues. The clinical geneticist is also meant to

listen and observe carefully and to take the questions and problems, presented by the patients and families, back to the basic researchers, to be addressed by future research.

I personally chose to go into medicine because I liked working with people. I was drawn to clinical genetics in its infancy and therefore have experienced the time before we could provide many options for individuals with genetic diseases and disorders. Thirty years ago, medical genetics was considered an extremely exotic specialty. This seems hard to believe now that it has become central to understanding all of human biology.

I remember well my very first genetic counseling session when I started as a "real" staff person. It was a family with a child with spina bifida. At that time, amniocentesis was just being developed for the detecting chromosomal defects. Prenatal diagnosis measuring the alpha fetal protein in amniotic fluid was not yet available, ultrasound for prenatal diagnosis of morphologic abnormalities was unknown, and maternal serum screening programs were unimagined. In addition, the extensive heterogeneity that exists among neural tube defects had not been recognized. We knew nothing about the multisite closure model, and there was no recognition of the preventive role of folic acid. A family could only be told their empirical recurrence risk and given a description of the available types of birth control.

Part of the reason to mention that child with spina bifida and its family is to make you aware of the progress that has occurred in the last 30 years. Each year there have been new options, new information, and new interventions to offer those families. It is through the combined and collaborative efforts of all of us, clinicians and basic scientists, that progress is made. Always we have to remember that we are working for real people. People like you and me. People with hopes and feelings. They are not just pages in a book. They walk through the door of a clinic asking for help.

Genetic Counseling

Genetic counseling always involves an exchange of information between the counselor and the family concerning a particular condition(s) and a particular family situation in a manner that the counseled individuals can understand the options available to them. As a result of that exchange of information, counselors also learn a new perspective, a solution, an insight from the counseling session, and can then share it with other families. I have learned over the years that most families believe they have only one option before coming to clinic. Genetic counseling broadens their view, provides information, and helps them to come to terms with *their* unique situation and to make decisions that are right for *their* family. The nondirective approach used in clinical genetics is quite different from other elements of medical practice where instructions and advice are the norm. Although the nondirective, nonjudgmental approach is expected as part of genetic counseling in North America and Europe, a different standard of practice exists in much of the world. Note the recently proposed eugenics laws in China, which would be considered draconian by our standards. In this approach, clinical geneticists try to imagine themselves in the position of the family, put themselves in the family's shoes, and then, with all their own background and knowledge as a clinical geneticist, think of the questions the family could or should ask. Most families are not in a position or frame of mind to know what to ask, even though the genetic problem they face can be the most devastating event of their lives. There is always a new perspective, a different model, that can be transferred from another disorder to share with a family and never a simple right answer or single way to think or plan.

It is an enormous privilege to observe the resiliency of the human spirit. I never cease to marvel at how families and individuals are able to deal with incredibly difficult situations. Although about one half of the families we see come apart, the other half expand their understanding of the complexity of human existence. It is predictable that they (the family and the individuals) will go through a series of reactions (shock, denial, anger, acceptance, and then constructive action), a process much like death and dying. Despite moving through different stages of this process at different rates, the families and individuals grow enormously over time with regard to their insights into the complex dimension of human experience.

I remember in my early years as a clinical geneticist meeting a marvelous family with a Down syndrome child, who said that the child was "such a blessing—a gift sent from God." At the time, I rather cynically thought that description was superficial, rather idealistic, and a sign of denial. Thirty years later, I have come to realize that many families and individuals do grow, accept, and rise to the challenge, change their view of the world, deal with new situations, gain new insights, and find their own personal way of dealing with adversity. Some even find that process of growth and change invigorating. It would be a great loss if the opportunity to follow an individual or family over time, and to learn from them, was sacrificed in a health care system that is driven primarily by economic considerations.

Most families faced with difficult decisions benefit from the chance to talk to another family with the same problem. There is a very special kind of communication that is possible through the lay support groups that are proliferating around the world (Alliance of Genetic Sup-

port Groups 1995). More information is available via E-mail at alliance@capaccess.org or by phone at 800-336-GENE.

These lay support/advocate organizations play many important roles. They can be enormously helpful in providing information for families at a level that is understandable. Such groups usually promote public awareness about the disorder, raise money to support research about the disorder, and strive to improve care for affected individuals. Most form an international network of advocacy and communication. They often have monthly or yearly social meetings, which can be a particularly important way to provide information and support to newly diagnosed or complicated families.

Clinician Researcher

An underlying theme for a clinical geneticist is to "treasure the exception," the unusual case. When faced with a challenging patient, the clinician becomes partly a researcher and is doing several things at the same time. He or she is collecting and sorting information in order to come up with an accurate diagnosis. Inherent in the diagnosis is an effort to understand the basic mechanism leading to the disease process. Concurrently, the clinician will try to provide appropriate therapy and prevent complications using the medical model. At the very same time the clinician deals with the complex nature of the psychosocial needs of the affected, the family, and the caretakers. The basic tenet in clinical genetics is that diseases occur because something—some pathway—goes awry, is not working, because some substance is missing, or in excess, or the timing is wrong. By studying the abnormal, we learn about what is necessary for normal function. The challenge in this modern molecular era is to make phenotypic/genotypic correlations. However, for the most part, clinicians are still dealing with the phenotype and the imprecisions inherent in describing traits. So little is understood about the processes of genetics diseases and about the process of personal growth. Only about a third of the families that present to a genetics clinic clearly fit into a specific diagnostic category or a specific counseling scenario. This next decade will surely witness a transition as we go past the phenotype into the genotype and then on to understanding pathogenesis. For the clinician scientist/researcher, the clinic is the laboratory in which to study these processes and acquire new knowledge by careful observation.

One of the real challenges within The American Society of Human Genetics is to appreciate the differences in the ways in which basic science researchers and clinicians function (see table 1). Each has their own way of dealing with unknowns. The approach of the basic scientist is to formulate a hypothesis and then gather information that will prove or disprove it. The approach of the clinician is to gather information in order to make a diagnosis, which one hopes leads to therapy. One approaches what is unknown. The other uses what is known. One is more theoretical. The other tends to be more applied. The basic scientist is usually in a laboratory, while the clinician spends most of their time with a patient or affected individual in clinics. Both approaches are useful and make important contributions to our knowledge, but they are fundamentally different. These two different approaches may come into conflict when involved professionals do not appreciate that, although there are differences in their goals and approaches, they are at the same time complementary.

Table 1

Human Genetics: Functions of Basic Science Researchers and Clinicians

Researchers	Clinician
Science	Medicine
Scientist	Clinician
Hypothesis driven	Diagnosis driven
What is not known	What is known
Theoretical	Applied
Bench	Bedside, clinic
Cells, molecules, animals	Humans

During this time of intense work on the human genome, an integral part of the process is the appropriate collection of cases and samples by the clinician. If, for instance, a disease gene is to be mapped, it is essential to be sure that a family has actually been diagnosed correctly. The ability of clinical scientists to make an accurate diagnosis is a very important and hard-won special skill that deserves appropriate recognition and acknowledgment.

More important, the accurate clinical descriptions of unique patients are often not included in molecular papers or are submitted separately. If this practice is perpetuated, there are likely to be significant problems in distinguishing phenotypic and genotypic heterogeneity, which will impede our understanding of the pathogenesis of specific genetic diseases.

The success of clinical research depends on the skills of the clinicians. It is a frightening prospect that without clinical training programs there will be few clinicians in the future who can actually recognize and diagnose the more than 5,000 disorders and syndromes that have been described; or who understand and recognize the complexities of genetic disease and their processes. The lack of funding for clinical genetics training programs capable of producing well-rounded clinical geneticists is quite distressing. In North America, the future of clinical geneticists is in real danger.

Natural History

To introduce my own research and my particular areas of interest, I would like to discuss the natural history of genetic disorders (Hall 1988*b*). As a clinician, clinician researcher, clinician scientist—the clinic has been my laboratory with its own set of guidelines, protocols, standards, and institutional review board—I have been involved in a variety of studies of natural history, including disproportionate short stature, Turner syndrome, arthrogryposis, and neural tube defects. The medical complications, the physical changes to be anticipated over time, and the life span of the individual are the information a family wants and needs. Initially they often do not care nearly as much about recurrence risks as they do about what is going to happen to this affected individual.

Studying natural history requires time and long-term commitment (usually unfundable, in our present milieu). Knowledge of natural history can lead to a correct diagnosis at various ages. For instance, an individual with Noonan syndrome looks quite different as an infant, a young child, an older child, an adult, or an elderly person (Allanson et al. 1985). In order to make the diagnosis at different ages, the differences have to be delineated and described.

The good clinician may recognize the unusual case, an unexpected clinical course, an undescribed complication that then allows a new group of patients to be distinguished—which may be attributed to a different allele, a different locus, a different type of genetic control, or gene interaction. The recognition of clinical heterogeneity and coming to understand the different mechanisms of disease may be the result of the study of the natural history disorders. Describing the natural history of a disorder also allows for the delineation of complications and their prevention or management. In order to evaluate the effect of a new therapy the "normal" course of the disorder must be known.

Genetic counseling, of course, depends on an accurate diagnosis but also requires knowledge of the mode of inheritance (or empirical observed risks). It will also require an explanation of what is to be expected over time and what options there are to deal with the complications.

The study of natural history helps to elucidate the mechanisms of pathogenesis, since the disturbances associated with an abnormal gene must be explained. As the knowledge of natural history has become sufficient to offer diagnosis, therapy, and prevention, human genetics has moved into the medical field and become a legitimate medical specialty. Now that the complete sequencing of all human genes seems truly possible, the real challenge will be to understand what controls genes and orchestrates their interaction.

Nontraditional Inheritance

As a clinician in a busy clinic, I have found that perhaps only a third of all patients seen fit into the traditional genetic explanations of extra or missing chromosomal material, a single-gene mutation, or the classical form of multifactorial disease. It is interesting to note that, when Mendel had the insight to describe units of heredity (single-gene inheritance) using pea traits, he cleverly ignored what did not fit. Only about a third of pea traits actually follow Mendelian rules. With the advent of molecular genetic techniques that give the ability to trace genes from one generation to another, and from one tissue to another, has come the growing recognition that there are many additional mechanisms of disease.

As we begin to recognize "nontraditional" mechanisms in genetics, they have become important ways to explain the unusual patient and family. In 1995, it is possible to make a list of the "new" mechanisms that have been recognized in the last 5–10 years. There will be many more. Mitochondrial diseases are only one example of cytoplasmic inheritance. It seems quite possible that other structures of the cell are influenced by structures in the egg. The maternally inherited template probably sets the pattern for many structures within the cell, such as the cell wall, the folding of proteins, and the shape of various organelles.

Mosaicism has been recognized to be present in all multicellular multiorgan organism. The new insight is that there are many types of "mutations" or changes that can be observed. They include DNA changes of single genes (both coding and noncoding domains), chromosomal loss or duplication, loss of X inactivation, imprinting loss or gain, loss of heterozygosity, etc. A second, a third, and fourth cell line may develop as well (Hall 1988*a*).

The concept of genomic imprinting is less than a decade old and yet has become extremely important in understanding gene control, pointing out parent-of-origin effects, and looking for specific molecular mechanisms to explain how differential control can occur (Hall 1990). Uniparental disomy, once thought to be an extremely rare occurrence, now explains many unusual observations and is likely to occur in conceptions starting as trisomies, i.e., zygote rescue.

Unstable mutations, such as triplet repeats, are being recognized as a common form of mutations, interestingly affecting the nervous system in a different way than the rest of the body. There are likely to be other mechanisms of mutation not yet imagined. Thus, we have probably just begun to understand the impact of nontraditional modes of inheritance.

Parent-of-Origin Effects

Until recently, parent-of-origin effects were conceptualized as maternal environmental influences during mammalian embryological development. During the last

decade, we have begun to find that many normal developmental processes involve parent-of-origin differences, and this finding offers an explanation for a number of unusual clinical observations. Recognized parent-of-origin effects in humans are as follows:

- Cytoplasmic inheritance
- Chromosomal deletions
- Single-gene mutations
- Trisomies
- Uniparental disomy
- Pairing
- Condensation (compaction)
- Recombination
- Late replication
- Genomic imprinting
- Allelic expansion
- Somatic recombination

Equally important as the list of these recognized parent-of-origin effects is the continued curiosity about this phenomenon. For years we have tended to put on blinders and have failed to ask some of the most fundamental questions in this area. The difference between the male and female contribution is important at many levels and throughout the individual's life. The different contributions are of course complementary and essential.

Feminine Qualities in Science

I want to emphasize one other perspective about science in the latter half of the 20th century. There has been a dramatic change in our society, with encouragement for women to assume leadership roles and to take on responsibilities outside the family circle. This is true in both science and medicine. The approaches that women have traditionally taken are adding new important dimensions to science. They are often traditionally feminine approaches (and of course many men have them as well). I realize this is a sensitive and politically charged area, but I think these traits are important, perhaps even correctives.

The feminine approach traditionally has been holistic (as compared to reductionistic), considering the whole organism as well as its parts. The whole is definitely greater than the sum of the parts. The whole organism is also more complex and interactive. Of course, in science it is important to understand those complex interactions.

A mentoring, nurturing approach has been the traditional one for those who raise children and produce the next generation. Many fathers know that role as well. I do not think this a male/female situation; rather, there is a need for team building as science moves into the 21st century. The amount of interdisciplinary work is increasing, and the need for large teams to be able to work cooperatively on problems has become evident.

There is also, of course, a need to mentor the mentors. Many of us had wonderful mentors, but not everyone learned mentoring skills. In the old days, intellectuals took time to reflect and meditate. Today, if you close your eyes, you miss a new paper or the sequence of a gene. Not all change is progress. The mentors need time to "smell the roses," too. At some time, everyone must have the chance to slow down and reflect—to refocus and rechart his or her course. Study leaves, sabbaticals, and administrative leaves are not a sign of weakness—but rather signs of maturity. Time for family, time for ourselves, is a sign of health. We must choose what not to do and take some time to find creative nontraditional ways of doing things. Just because it can be done, does not mean it should be done.

In science, a nurturing approach is particularly important for trainees. The "sink-or-swim" mode is outdated. Part of nurturing children has been to socialize them, teach them manners, social skills, and culture. This includes an awareness of ethical issues. Today in science that translates into a concern about the social and ethical ramifications of our work. It also relates to building teams, working together, and awareness of the values inherent in our science culture.

The feminine approach has been to emphasize process. To be sure that everyone understands and is included. Today, that has translated into networking and inclusiveness that is currently facilitated by our modern information technology.

Science is supposed to be objective and numerical. However, new subjective approaches are being developed to describe complex interactions in the social sciences (in basic science as well). There is also room for pursuing intuition while using the scientific method. I will never forget reading Barbara McClintock's description of herself—frustrated by not understanding her data, she went for a walk, sat down on a bench and said to herself, "Now if I were corn, how would I do this?" For the moment, she "became the corn." Then she realized, felt, knew, and had the sudden insight to understand her results—which, of course, represented a new mechanism of inheritance involving transposable elements. For these insights, she was awarded the Nobel prize (Keller 1983).

A peacemaking collaborative approach in science includes the development of the teamwork that is needed for complex science. Mothers cannot stand fighting kids, and so they are very inventive at developing dispute resolution methodologies and patching up bruised knees and feelings. Our world needs more peacemakers, and we must learn to work collaboratively. Genetic science is becoming too complex to do alone. It requires groups and interdisciplinary approaches—acknowledging the special skills of each individual. "No man is an island," and today we recognize that no human being, no scien-

tist, can work in isolation. This type of teamwork and interdisciplinary interaction takes a new set of skills in balancing fairness with a businesslike approach. There is a need to train individuals to work in groups. This approach will be even more important in the years to come. Someone commented recently that the number of authors on genetic papers is getting close to the number on astronomical physics papers. To solve the complex biological challenges in genetics, we need supportive collaborations and multidisciplinary interactions.

The feminine approach has been to care about the physical environment in which we work and in which we live. Conservationists remind us to protect endangered species and their natural habitats, but we need to care also for the spaces in which we provide counseling for families, the safety of the laboratories in which we work, and the surroundings in which we have conferences. We all must be concerned about our environments in order to preserve and keep them human "friendly" for the long term.

The research subjects that women choose are often somewhat different from those of men. That is not to say that women bring any less rigor or commitment in the intellectual pursuit of science, but rather they may bring a different set of values, a different perspective and different areas of interest.

The very language that is used to describe things may be different, and language greatly affects perception. So, we find ourselves instead of talking about X inactivation in man, talking about X inactivation in humans. Meaning, of course, this is something that happens to female human beings.

Catching Them Early

I am a clinical geneticist because I was introduced in undergraduate days to genetics by a wonderful woman, Miss Austin, who loved genetics with a passion. Paramecia and fruit flies were her thing, and her enthusiasm was contagious. I was very fortunate to have taken an elective with Arno Motulsky in my first year of medical school. He made medical genetics come alive and convinced me research was so much fun that I should do a master's degree in his laboratory. I went on to do a fellowship with Victor McKusick, who had a vision of mapping the whole human genome before any of the rest of us even knew the word "genome." I believe in early inoculation—the infection works best that way. A species survives only if it is fertile and has lots of offspring. Institutionally sponsored summer student research programs and public and high school education programs like the ones the Society has sponsored so successfully the last few years are part of our responsibility.

Changes for the Geneticist

I remember my first day of medical school, the dean welcoming us and warning us that in 30 years only 10% of what we were about to learn would still be correct and relevant—so that we needed to learn, to think, analyze, and critique. At the time it sounded like old fuddy-duddy talk—so either I have become one or have recognized the inevitability of needing to be able to live with change. In fact, without change, one is dying, and the lovely discovery for me about being an adult is that one gets to continue to grow and change.

Currently the human resources experts warn us that over a lifetime our jobs will change at least 10 times, and we all must be flexible and acquire new skills. Although I think of myself as a clinical geneticist, in actual fact I have been a student, a laboratory scientist, an internist, a pediatrician, an endocrinologist, a clinic manager, a department chair, a health care planner, a patient advocate, a media consultant, a writer, an editor, and an executive in many professional organizations. The highlight of course, is to be president of this organization. Each job requires different skills, training, and new ways of thinking.

The American Society of Human Genetics within a World That Is Changing

One of the hats I wear in The American Society of Human Genetics is that of a Canadian. I emigrated from the United States to Canada 15 years ago, and this has given me a unique perspective and an understanding of how differently various countries go about doing their business. It has allowed me to appreciate the really fine research that is done all over the world, a perspective that many Americans are just beginning to develop. It also makes me specifically aware that The American Society of Human Genetics is a society of all of North and Central America and even includes South America. We have a responsibility to address the political, clinical, and research needs of all of our constituents north and south as well as within the U.S. borders. The American Society of Human Genetics is a world leader and has much to share. While remembering that the North America way is not the only way—and our values are not necessarily the values of the rest of the world—we, as a Society, and as society members, have many opportunities to contribute and make a positive impact.

Changes in The American Society of Human Genetics

Now that you know who I think I represent in being your president, it is time to shift and talk about The American Society of Human Genetics itself and the processes that it has gone through in the last decade. As you well know, our society has supported and encour-

aged the development of a group of organizations: the National Society of Genetics Counsellors, which then developed its own board; the International Society of Nurse Geneticists; the American Board of Medical Genetics; the American College of Medical Genetics, which then developed its own foundation; the Association of Professors of Human or Medical Genetics; and the Consortium of Professional Women in Genetics. Many other groups working in genetics and those concerned with human and medical genetics come together in COMGO, the Council of Medical Genetics Organization. By encouraging the development of these groups, the Society is now able to refocus on the scientific aspects and scientific questions of genetics. Just as when parents watch their children grow up, they change their view of the world and become concerned about its future because their children will be living in it, so The American Society of Human Genetics is watching the development of these new groups with pride and concern about the future.

There are three major functions of the Society: the annual meeting, the *Journal,* and the work of the committees. The Board is looking for ways to enhance and strengthen each and to make them more useful to the membership.

The American Society of Human Genetics Board of Directors has gone through a process this year of reaffirming our emphasis on research and education as well as reaffirming that our strength comes from the diversity of different kinds of geneticists who interact and take part in this Society. Your Board has also defined two major goals for the future. The first one is to increase communication among all of the members and other genetic groups. The Society has developed a page on the World Wide Web to provide information about North American genetic groups including their statements and guidelines (http://www.faseb.org/genetics/ashg/ashg-menu.htm). We have established liaison representatives with a number of groups related to genetics. We have developed the mechanisms to produce policy statements in a timely fashion.

The second goal is to find ways to involve the young Society members and trainees—our colleagues of the future. We care about them and want them to play an active part in the Society. We are looking for their ideas about improving our Society. It is quite clear that our Society gains strength because of the many different types of geneticists composing our membership. We live in a time of change in which the knowledge in the field of human genetics is exploding, making it next to impossible for a single individual to keep up. We need our Society to be interdisciplinary in this time of change.

Reflections on Change

Let me close by reflecting again on change. Change is said to be as inevitable as death and taxes. All living organisms change. It is clearly a sign of being alive to experience change. I think we all feel a bit threatened by changes over which we have little control. Although it is a Chinese curse to live in times of change, change brings great opportunity as well. "Change," of course, can be a verb, a noun, or an adjective. As a verb, Webster (Merriam-Webster 1987, pp. 224–25) defines it as "to make a difference; to become radically different; to transform; to give a different position, course or direction; to replace with another; to make a shift from one to another; to switch; to exchange for an equivalent sum; to undergo modification; to put fresh clothes or fresh covers on; to transfer; to become different; to pass from one phase to another."

As a noun, "change" has a slightly different meaning: "the act, process, or result of changing; an alteration and transformation; a substitution; a passage; a fresh set of clothes," while as an adjective "change" means "capable of change; subject to change."

In fact, within that context, of course, we in genetics, in human genetics, in The American Society of Human Genetics, are undergoing change, and these definitions suggest a very positive process. The very essence of science is to ask the right questions, which lead to changes in understanding.

Our social fabric is changing around us as well. To be relevant, we have to bring new information to bear and to integrate it into society. Therefore, one of the real challenges we face is to be relevant to society. The ethical issues that scientific work stimulates are really societal issues. We have a responsibility to be sure that the public knows enough science to understand the concerns and choices that need to be made. So in this time of change there is need to ask new questions and challenge old adages. Change is a time of great opportunities.

I want to close by talking to the younger among us and letting them know that working in the field of genetics provides an incredibly exciting and wonderful opportunity. No matter what background you come with, or title you claim, the future for work in human genetics is sure to be challenging and stimulating. However, with change comes uncertainty, and you may hear the moans and groans about funding, job insecurity, and working conditions, but that is true for every profession. However, not every profession has the excitement of being part of a new way of thinking, a way of thinking that is being adopted by every part of science and every specialty in medicine. Not every profession can be at the cutting edge of understanding and application. Not every profession can try to answer the profound questions of biology. We do live in exciting times. We live in times of changes, and these are times of great opportunity. Thank goodness it affords each of us the chance for positive and creative change. In both our personal and professional lives.

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